the presence of an active tuberculous focus, although there may be no symptoms of the disease present.

7. Positive results are obtained in a large percentage (66 per cent.) of clinically inactive cases of pulmonary tuberculosis, and such a result indicates that though it may be quiescent the infection has not disappeared.

8. The results obtained with the test described are practically as good as those obtained with the Wassermann test for syphilis.

Of course, much more work is needed before this, or any other method of diagnosing tuberculosis by complement-fixation is placed upon a thoroughly practical basis and is generally accepted as a routine diagnostic measure, but it is confidently believed that continued work upon this subject will result eventually in the perfection of a test that will be fully as useful in the diagnosis and control of the treatment of tuberculosis as is the Wassermann test in syphilis.

I desire here to express my thanks to Doctor Edward R. Baldwin for seven strains of the human tubercle bacillus kindly furnished me from the Saranac Lake Laboratory, and to Dr. Simon Flexner for three strains of the bacillus from the Rockefeller Institute. The antigens used in my experiments were prepared from six of the strains furnished by Dr. Baldwin and one of the strains furnished by Dr. Flexner.

LANDRY'S PARALYSIS: REPORT OF A CASE WITH NECROPSY AND HISTOPATHOLOGICAL FINDINGS.[1]

By Edward D. Fisher, M.D.,
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Many cases have been reported since Landry first described a disease characterized by a rapidly ascending paralysis passing from the lower to the upper extremities, thence to the cranial nerves, causing various paralyses, and ending fatally in the course of six or seven days with involvement of the vagus and respiratory failure. The pathological changes in the early cases were negative. This may have been due to the insufficient method of examination in part, but even in later reports very few changes have been found at times.

In the literature of this subject, which is considerable since Landry, in 1859, described his case, we find various lesions recorded in which either polyneuritis or spinal cord or bulbar inflammatory involvement has been present, or all in combination. Leyden and

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[1] Read before the Americal Neurological Society, New York City, May 8, 1915.

Goldscheider are among those who support this view. The cord changes are usually hyperemia, perivascular and pericellular infiltration, and hemorrhages into the gray and white matter; at times an interstitial and parenchymatous neuritis with or without cell involvement in the cord and bulb. The latter type is rather the exception than the rule. Our case belongs to the neuritic type with involvement of cells of the cord and brain stem.

E. Lugaro made an exhaustive study of reported cases of Landry's paralysis of the neuritic type up to 1904. He prefers to designate Landry's paralysis as a clinical entity characterized by an acute ascending flaccid paralysis, irrespective of pathological findings. And he cites cases of a purely neuritic type of Centanni, Eisenlohr, Leyden, Thomas, Reusz, Krewer, Wochenius, Roth, Rosenheim, Nauwerk, and Barth. All of their cases presented the same syndrome, namely, an acute ascending flaccid paralysis. Besides the interstitial and parenchymatous neuritis, there were also cell changes in the anterior and posterior horns of the cord. But these were of a reactionary type, due to remote influences in their neuraxones.

All authors agree that the disease is of infectious origin, and attempts have been made to isolate a specific organism, but without success. Centanni isolated a bacillus from the nerve trunks, Eisenlohr a Staphylococcus pyogenes and a Staphylococcus cereus albus from the spleen and sciatic nerve. Leyden's case came on after influenza. Wochenius found a Staphylococcus pyogenes albus in the spleen and peripheral nerves. In some cases pulmonary tuberculosis was a complication. Lugaro goes so far as to classify the cases reported by Korsakow and Serbski as puerperal polyneuritis, and similar ones reported by Prybitkow and one by Mader, as Landry's paralysis, because of the clinical picture.

Because of the fact that there is no specific agent causing the affection, he is inclined to advance the hypothesis that the toxin alone is responsible for the extensive destructive changes in the nerve tissues, and that in some cases only both the virus and its toxin are at work. He also points out that the time element as to the duration of the disease is not material for it may last a few days or a few weeks.

Since 1904 several other cases were reported that approximate my case both as to clinical and pathological data. Among them Pfeiffer, Burghart, Mosny and Moutier, and others report such types. The cases of Burghart and of Mosny and Moutier were complicated by pulmonary tuberculosis and lasted four weeks and two months respectively. In none of these cases was any germ isolated. Levaditti has injected a monkey with the emulsion of the cord of Moutier's case, and obtained negative results.

The case I shall record may be of interest, as it was observed from the onset, and a careful postmortem examination has been made.

Case Report. W. E., boy, aged fifteen years. Family history is negative. With the exception that he was operated upon for an inguinal hernia two years before his present illness, his personal history is negative.

Present Illness. September 27, 1913, he complained of a sharp pain in the calf of the left leg. This pain was gone the next day, but left him with a weakness in both lower extremities. He was able to walk without much difficulty but favored his left leg, holding it somewhat bent to keep him from falling. This condition grew progressively worse until October 11, when he was admitted to St. Vincent's Hospital, in the service of Dr. Constantine J. MacGuire. His paraplegia was then complete and he had to be carried to the hospital.

Status on Admission to the Hospital. Patient was well developed and a little above the average height for his age. The temperature was 99.2°, pulse 72, and respirations 24.

Examination of heart, lungs, and abdominal viscera was negative.

Muscles of the head and neck and of upper extremities were normally active. There was a flaccid paralysis of the lower extremities, with loss of reflexes and pain on pressure over the large nerve trunks. There was no dissociation of touch, pain, or temperature sense. No anesthesia. Deep muscle sense was normal.

Laboratory Findings. Urine, amber color; acid; specific gravity, 1019; albumin and glucose negative; no casts; no crystals. Blood: leukocytes, 23,500 per cubic millimeter; polynuclears, 86 per cent.; transitionals, 2 per cent.; lymphocytes, 12 per cent. Spinal fluid clear and colorless; normal pressure. Fehling's reduction test positive; globulin slightly increased and 7 cells per cubic millimeter. Smears and cultures negative for bacteria. Wassermann reaction negative in blood serum and spinal fluid. Throat cultures negative.

October 15. Patient vomited and complained of severe abdominal pain and chilly sensations. Blood culture taken and proved negative. The pain and vomiting were relieved by catharsis and colonic irrigation.

October 17. Complains of seeing double and holds the left eye closed so as to prevent it. Paralysis of left external rectus. Dr. Kelly examined the eye-grounds and found them to be negative.

October 25. Restless the greater part of the night and complains of pain in the left shoulder. Has a headache and vertigo and vomited after lunch. From this time he had a progressive weakness and loss of power in arms and hands, until in about one week it was complete.

October 29. Headache is gone, but complains for the first time of some difficulty in swallowing. Dr. Kelly reports now complete paralysis of the muscles of the right eye and of the superior oblique of the left.

November 1. Blood count: leukocytes, 5900; polynuclears, 60 per cent.; lymphocytes, 38 per cent.; basophiles, 2 per cent.

November 3. Complains of pain in the cardiac region.

November 9. Again had difficulty in swallowing, and had pain in the back and temporary shortness of breath.

Neurological Examination. Cranial nerves: I, unaffected; II, negative; III, left normal; almost complete right-sided palsy; right ptosis; pupils react to light and accommodation well; IV, left paralyzed; V, right affected; diminished sensation of cornea and right side of face; weakness of masseter; VI, left paralyzed; VII, bilateral facial paralysis of the peripheral type; unable to wrinkle forehead, show teeth or close eyes tightly; difficulty in pronouncing consonants "b" and "p"; VIII, IX, and X, normal; XI, affected; trapezii and sternomastoids weakened; XII, normal. Motor functions: double foot-drop with complete loss of power in legs, flexors, and extensors being equally involved. Double wrist-drop. With the exception of slight movements of fingers, almost complete paralysis of upper extremities. Muscles of trunk markedly involved.

Sensory functions: Coördination, deep muscle sense normal. Decreased touch and temperature sense.

Trophic disturbances: Marked atrophy of muscles of lower extremities. Slight atrophy of muscles of arms and hands.

Reflexes: K. J., A. K., W. K., E. K., absent. Abdominals present. Pupillary normal. Sphincters normal.

Electrical reactions: Absence of faradic response and R. D. present in lower, quantitative and qualitative diminution in upper extremities.

November 17. Marked shortness of breath, respirations 40, almost wholly costal. Pulse, 90. First valvular sound impure, second pulmonic accentuated. Pulmotor had to be used to relieve dyspnea. Pulse went up to 150, and was weak and thready.

November 21. Patient died of respiratory failure.

Necropsy. Dr. John H. Larkin made the autopsy and reported that the thoracic and abdominal viscera were normal. The cord showed an intense congestion, but otherwise was macroscopically negative. Sections of the sciatic nerve, cord, medulla, and pons were prepared by him and studied by Dr. M. Neustaedter, who makes the following report on the histopathology of the case:

MICROSCOPIC STUDY. Sections of all levels of cord, medulla, pons, and the sciatic nerve were examined. These were stained according to the methods of Nissl: toluidin blue and polychrome methylene blue; Van Gieson, Mallory, Bielschowski, Weigert-Pal, Nigrosin stain; Marchi and Sudan III.

Spinal Cord. Sections from the lumbar, dorsal, and cervical segments. The cells of Clarke's column show a central chromatolysis, with remnants of small, narrow, and poorly defined and darkly staining bodies lining the periphery of the cells. The protoplasm of the remaining cell is a diffused granular mass assuming a faint stain and giving the cell a dusty appearance. The cells are markedly swollen, and nuclei, when present, are eccentrically situated. The nucleoli stain rather darkly and under high magnification show a disintegration of their substance into bodies of various shapes and sizes. The cell prolongations are everywhere faintly stained. This degeneration is manifested in all the cells of Clarke's column at all levels of the cord. Nowhere along this column is any evidence of a neuronophagocytosis to be found, although there is a fair amount of hyperplasia of glia cells in their vicinity.

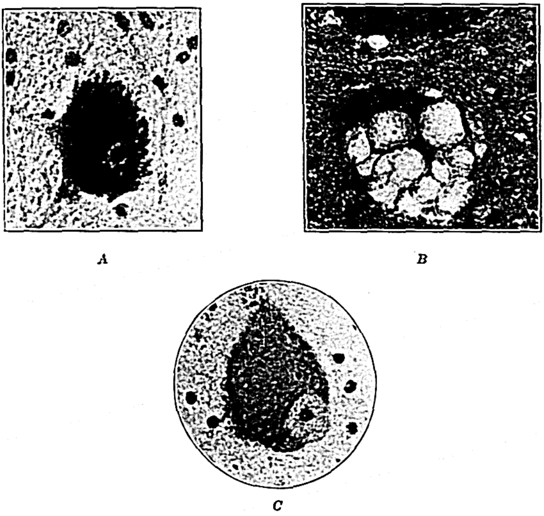

Fig. 1.—*A*, degeneration of anterior horn cells, showing a tygriosis and a beginning chromatolysis around the periphery, with eccentric nucleus. Nissl stain. Zeiss, 8 mm. Oc. 6. × 450. *B*, cell vacuolization of anterior horn cell. Van Gieson stain. *C*, degeneration of cells of Clarke's column, with central chromatolysis, chromophilic substance lining the periphery. Nissl stain. Zeiss, 16 mm. Oc. 3. × 60.

The large multipolar cells of the anterior horns throughout all the segments of the cord are seen to have undergone three forms of degeneration of various intensities. The most prominent feature is a coalescence of the tygroid substance, a tygriosis, and a consequent shrinkage. The cells stain darkly or assume such an intense stain that the chromophilic substance cannot be differentiated at all. This condition cannot be an artifact or overstaining, since other cells on the same section are staining quite well. In assuming such a dark stain the cell obliterates the view of the nucleus if present. In some cells the nucleus is eccentric and its cytoplasm broken up into irregular bodies and the nucleolus is staining very deeply. The prolongations of these cells are visible and retain slight meshes of chromophilic substance. Around the periphery of the cells and at times dipping into the cell body itself are seen round cells, large and small, of the type of satellite cells. To a lesser extent we find cells in the anterior horns, with a central chromatolysis of the type described in the cells of Clarke's column. In cells affected by this phase of degeneration the prolongations are gone and no evidence of any neuronophagocytosis is present. Very rarely, indeed I have only seen it on three sections, there appears to be a cell vacuolization with the nucleus entirely gone and a slight neuronophagocytosis present. The first type of degeneration is most pronounced in the anterior horns of all the cervical and dorsal segments, while the second type is most pronounced in the anterior horns of all levels of the lumbar region and in the cells of the lateral horns all over the cord.

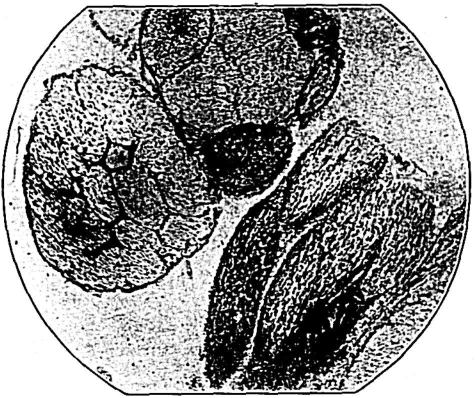

FIG. 2.—A diffuse and focal infiltration of leukocytes in the anterior nerve root, cervical segment. Nissl stain. Zeiss, 16 mm. Oc. 3. × 150.

The significance of these phases of cell degeneration has been established by pathological investigation and experimentation, namely, that a central chromatolysis with swelling and eccentricity of the nucleus, together with chromophilic substance present in well-defined meshes around the periphery of the cell, is accepted to be a reactionary degeneration or attempted regeneration of the cell as a result of a lesion remotely in the cell prolongation—in the neuraxone. While the degeneration beginning as a tygriosis, coalescence of the chromophilic substance accompanied by swelling in some instances, and a shrinkage or cell vacuolization following it in the presence of a more or less marked neuronophagocytosis and a gradual cell destruction in which the tygroid substance is present as long as a part of the cell is present is accepted as an inflammatory reaction within the cell itself, or its pericellular lymph space or in the substance of its immediate neighborhood. In the first type we see slight evidence of any remaining neuraxone or other cell prolongation, while in the latter type we always see a well-stained cell prolongation with some meshes of the chromophilic substances.

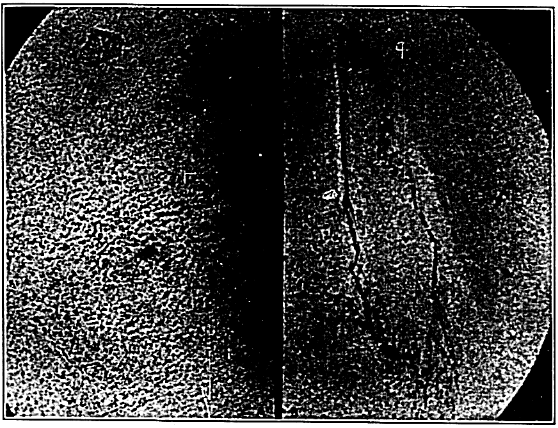

Fig. 3.—*A*, focus of marked glia-cell proliferation in the gray matter in the neighborhood of the aqueduct on a section through the red nuclei. Nissl stain. Zeiss, 16 mm. Oc. 3. × 60. *B*, slight perivascular infiltration of mononuclears in the same neighborhood. Nissl stain. Zeiss, same magnification as *A*.

In view of the fact that we have the first type of cell degeneration present to a great extent, and the second type only in some parts of the anterior horns, we should expect definite pathological changes in the peripheral nerves and a clinical picture in conformity with these. This discussion we shall leave to the end after first reporting the other findings.

Sections stained by the Bielschowski method show a marked degeneration of the neurofibrils of the cells of the anterior horn, while those of the cells of Clarke's column are entirely absent. This is true of all the levels of the cord.

There is a considerable hyperplasia of glia cells in the gray and white matter of the whole cord, and not infrequently do we meet with darkly staining, small mononuclear round cells, especially pronounced in the neighborhood of the blood vessels, filling in their perivascular sheaths to a very slight extent. They are most probably lymphocytes.

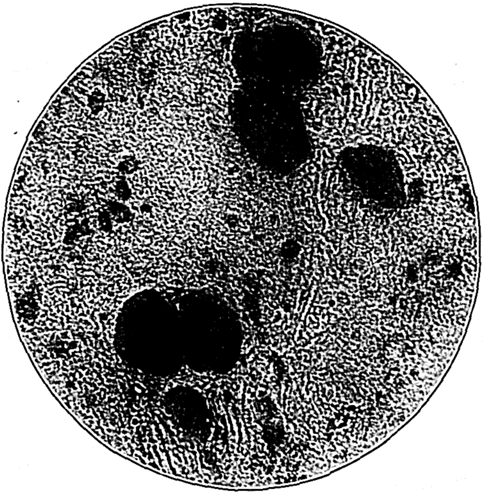

FIG. 4.—Swelling, central chromatolysis, and degeneration of the cells of the descending nucleus of the fifth. Nissl stain. Zeiss, 8 mm. Oc. 6. × 440.

A feature of considerable interest in this case is the ependymitis around the central canal, especially well established at the levels of the cervical and lumbar enlargements. We find here a considerable hyperplasia of ependymal cells with an intense infiltration of large polymorphonuclears around the central canal with not an inconsiderable amount of small, darkly staining mononuclears. At some levels of the cervical enlargement there are even some large polymorphonuclears found within the lumen of the canal.

Finally, it must be noted that the capillaries of the gray matter of the anterior horns are engorged. In many instances one notices capillary aneurysms, and not infrequently these burst and give rise to extensive hemorrhages. Hemorrhages of the white matter I have noticed only in a few instances in the posterior columns.

The Medulla and Pons. The cells of the nuclei graciles and cuneati show a pronounced degeneration of the type found in the cells in Clarke's column of the cord, while the cells of the motor nuclei and of the formatio reticularis show evidences of the type of degeneration we found in the ganglion cells of the anterior horns of the cord, namely, a tygriosis. Throughout the segment at the level of the decussation of the pyramids there is a fair amount of hyperplasia of glia cells and some diffuse and very slight perivascular infiltration of deeply staining, small, round mononuclears. The central canal shows here also some ependymitis as in the cord.

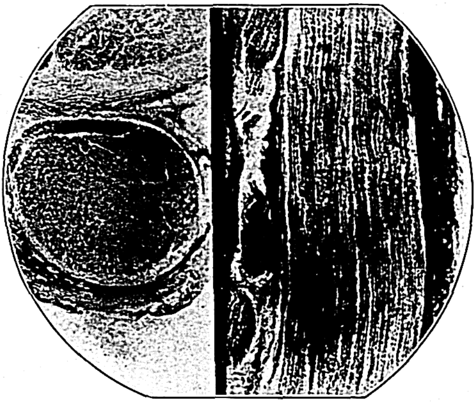

FIG. 5.—Longitudinal and cross-sections of the sciatic nerve, showing pronounced degeneration of the myelin substance. Marchi and Weigert-Pal stains. Zeiss, 16 mm. Oc. 3. × 60.

The cells of the nuclei of the third and sixth cranial nerves show the following form of degeneration. There is a central chromatolysis around the nucleus, which in most instances is at the periphery, while the tygroid substance of the remaining cell has undergone disintegration, appearing in irregular, thick, and broken meshes. The nuclei are swollen and stain very lightly while the nucleolus assumes a dark stain. The cell prolongations are visible. Many of the cells are gone for the greater part and no trace of the nucleus would be present. The capillaries are filled and in some instances there are thrombi present. These changes are also evident in the sensory nucleus of the fifth and the sensory as well as the dorsal nuclei of the tenth nerves. The nucleus ambiguus shows no change that I would consider pathological. The cells of the descending and ascending roots of the fifth are very much swollen and show a general chromatolysis with the protoplasm disintegrated into a fine granular mass giving the cell a peculiar dusty appearance. At the periphery there are still evident darkly staining tygroid bodies, and their neuclei when present are eccentric and swollen, staining very lightly with the nucleolus staining somewhat deeper. The cell prolongations of these cells are totally gone and there is no evidence of any peri-

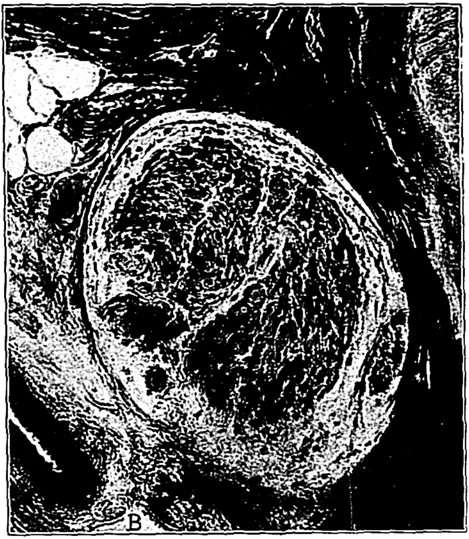

FIG. 6.—Cross-section of sciatic nerve, showing proliferation of the perineurium, extensive parochymatous degeneration of nerve fibers, and connective-tissue increase; infiltration of leukocytes and Gitter cells. Some thickening of the endoneurium and fatty degeneration of the perineurium. Mallory stain. Zeiss, 8 mm. Oc. 6. × 250.

cellular infiltration. The cells of the nuclei of the seventh and twelfth nerves show changes characteristic of the motor nuclei of the bulb at the level of the decussation of the pyramids. In the cells of the other pontine nuclei, the nuclei rubri, and basal ganglia show alterations similar in type to those of third. In the region of the nucleus ruber we find also some perivascular infiltration of mononuclears and endothelials, and also some focal infiltration of small, darkly staining mononuclears and polymorphonuclears as well as some hemorrhages. The glia cell proliferation is very much marked throughout.

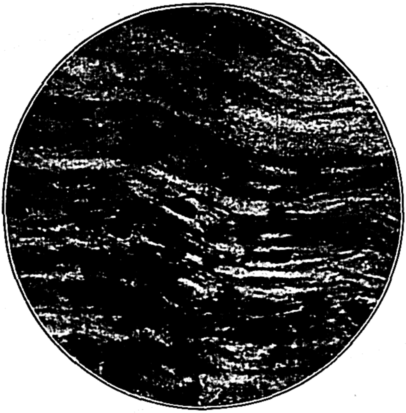

FIG. 7.—Posterior nerve root, lumbar segment showing polyblasts and some Gitter cells. Mallory stain. Zeiss, 8 mm. Oc. 6. × 400.

The spinal nerve roots of all segments stained by the Nissl method show at times a diffuse and at times a focal-cell infiltration into the lymph spaces of the epi-, peri-, and endoneurium. Those of the lumbar segments are most intensely affected. The anterior roots are far more involved than the posterior. This infiltration is not only evident in the distal end of the nerve trunks but also at the entrance of the nerve roots, and which consists of small, round, darkly staining mononuclears, fat granular cells, and polyblasts from which the latter are really formed. At times there is to be seen a hemorrhage into the posterior nerve root, the contiguous white substance of the cord, and into the pia. The thoracic segments are subjected to this change. There is also an infiltration of the perivascular lymph spaces at the nerve roots which consists of mononuclears and endothelials. The cross-sections of the anterior and posterior nerve roots stained according to methods of Marchi, Mallory, Van Gieson, Bielschowski, and the Nigrosin stain show markedly destructive parenchymatous and interstitial changes. It would seem that the toxic substance has been propagated through the perineural lymph spaces in a comparatively rapid time, producing such extensive and destructive changes. In other places we find a complete breaking down of all the elements of the nerve fiber, a thickening of the endoneurium, and a proliferation of the connective tissue.

The peripheral nerve studied is the sciatic. With the polychrome blue stain there is evident an infiltration of cells, but not as marked in the nerve roots. This infiltration is mainly pronounced in the peri- and endoneurium, and consists of polymorphonuclears, polyblasts, and Gitter cells. Here and there one finds a lymphocyte. The infiltration is most marked in the neighborhood of bloodvessels. There is also a slight proliferation of cellular elements, but their protoplasmic processes are not visible. The connective-tissue and endothelial cells are more proliferated than other cell elements. Especially on cross-section one observes a very marked connective-tissue cell proliferation with their protoplasmic processes extending to some extent between the nerve fibers. The Schwann cells are rather swollen. With the Marchi stain there is to be noted a degeneration of the myelin substance, forming irregular masses scattered throughout the nerve fiber. With the Van Gieson and Nigrosin stains a very extensive nerve fiber destruction is to be seen. The peri- and endoneurium appear markedly thickened, their vessels show a considerable infiltration into their lymph spaces, consisting of large and small round cells. Their endothelial coat is thickened and the endothelium loose. The proliferation of connective-tissue fibers and cells is quite evident. There is also a pronounced infiltration of polyblasts and Koernchenzelln among the fibers. The Schwann nuclei are swollen and stain deeply, and at times fairly occlude the lumen of the fiber. Some fibers show an obliteration of the axis-cylinder, and the myelin substance presenting masses filled with fine, dusty granules assuming a bluish tint with the nigrosin stain. Others, again, show no differentiating characteristics at all, but become confluent into a connective-tissue mass with a marked cell infiltration.

In view of such extensive parenchymatous and interstitial changes in the nerve roots and trunks the question comes up whether we are dealing with end results of a toxin or a bacterial activity, or of both. The cell infiltration would point to a bacterial invasion resulting in a phagocytosis along the lymph spaces of the nerves through which the virus was disseminated. In view of the fact, however, that the infiltration is not marked in all places alike, and in some instances it is rather slight, although the changes in the fibers are very pronounced, and in view of the fact that the duration of the disease was rather longer than usual, I hold that both the virus and the toxin did play an equal part in bringing about these changes in the peripheral nerves primarily, and these gave rise to the reactionary cell changes in the cord and medulla and pons. The ganglion cell changes, however, which are accompanied by a slight neuronophagocytosis are, in my opinion, the direct result of the virus.

CONCLUSION. We have here, therefore, a case of ascending paralysis, with attending neuritis, which followed the usual course of extension, later involving the upper extremities and bulbar nerves resulting in respiratory failure. The pathologic findings are definite, involving both the peripheral and central nervous systems. The course of the disease was longer than usually described, extending over six weeks, but otherwise the case was typical in its clinical manifestations.

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THE VALUE OF SYMPTOMATIC DRUG TREATMENT.

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As compared with a few decades ago, drug therapy occupies a less prominent place in the treatment of disease, and inasmuch as most of our medication is symptomatic in character, it probably means that symptoms are less frequently treated than in former years. Is this to be considered a step in advance, or are we, on account of our interest in scientific medicine, negligent of an important detail in treatment? It is probably true that with the development of specific drug therapy and biological products the physician has become more impatient with and less interested in treatment directed toward giving only temporary relief. Other important reasons, however, must be considered. The profession each year contains more and more men with careful scientific training. This